

Italian Cardiostim 2006 Symposium: Sudden Death Management in Sport

Controversial and Emerging Indications for ICD

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ICD therapy has proved to be very effective in prolonging survival in patients either survived to an arrhythmic event (secondary prevention) or at high-risk to develop it (primary prevention).

Secondary prevention trials:

- AVID
- CIDS
- CASH

Primary prevention trials:

- MADIT I
- MUSTT
- MADIT II
- CABG-Patch
- CAT
- DINAMIT
- AmioVIRT
- COMPANION
- DEFINITE
- SCD-HeFT

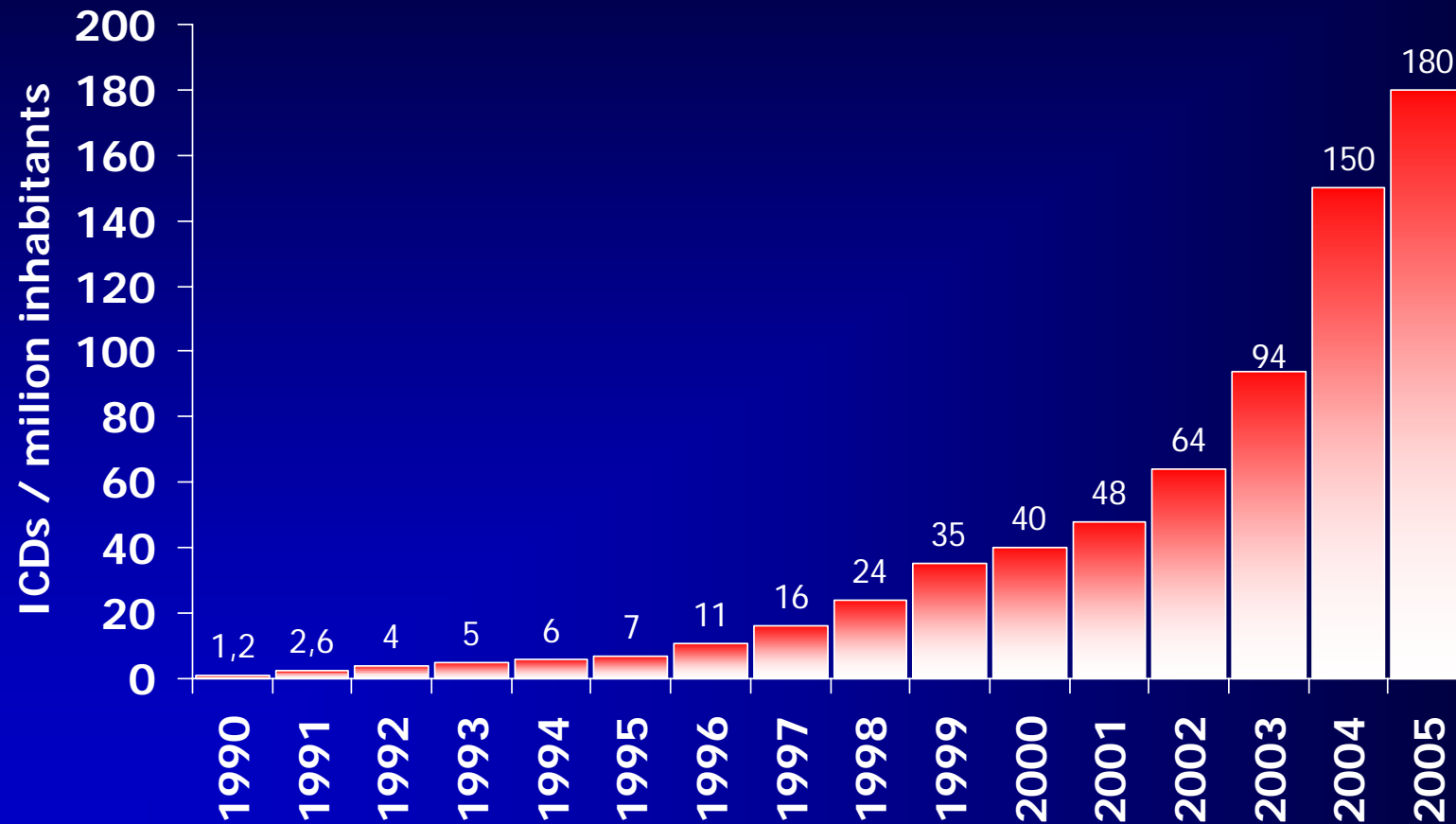
ACC/AHA/NASPE 2002 Guidelines for ICD

	Level of Evidence
Class I Indications	
Cardiac arrest due to VT or VF, not due to a transient reversible cause.	A
Spontaneous sustained VT in association with structural heart disease.	B
Syncopal of undetermined origin with clinically relevant, hemodynamically significant VT or VF induced at EPS when drug therapy is ineffective, not tolerated, or not preferred.	B
Non-sustained VT in patients with coronary artery disease, prior MI, and inducible VT at EPS that is not suppressed by class I antiarrhythmic drugs.	A
Class IIa Indications	
Patients with left ventricular ejection fraction $\leq 30\%$, at least one month post-MI, and three months post-CABG.	B

Gregoratos G, et al. *J Am Coll Cardiol.* 2002;40:1703–1719

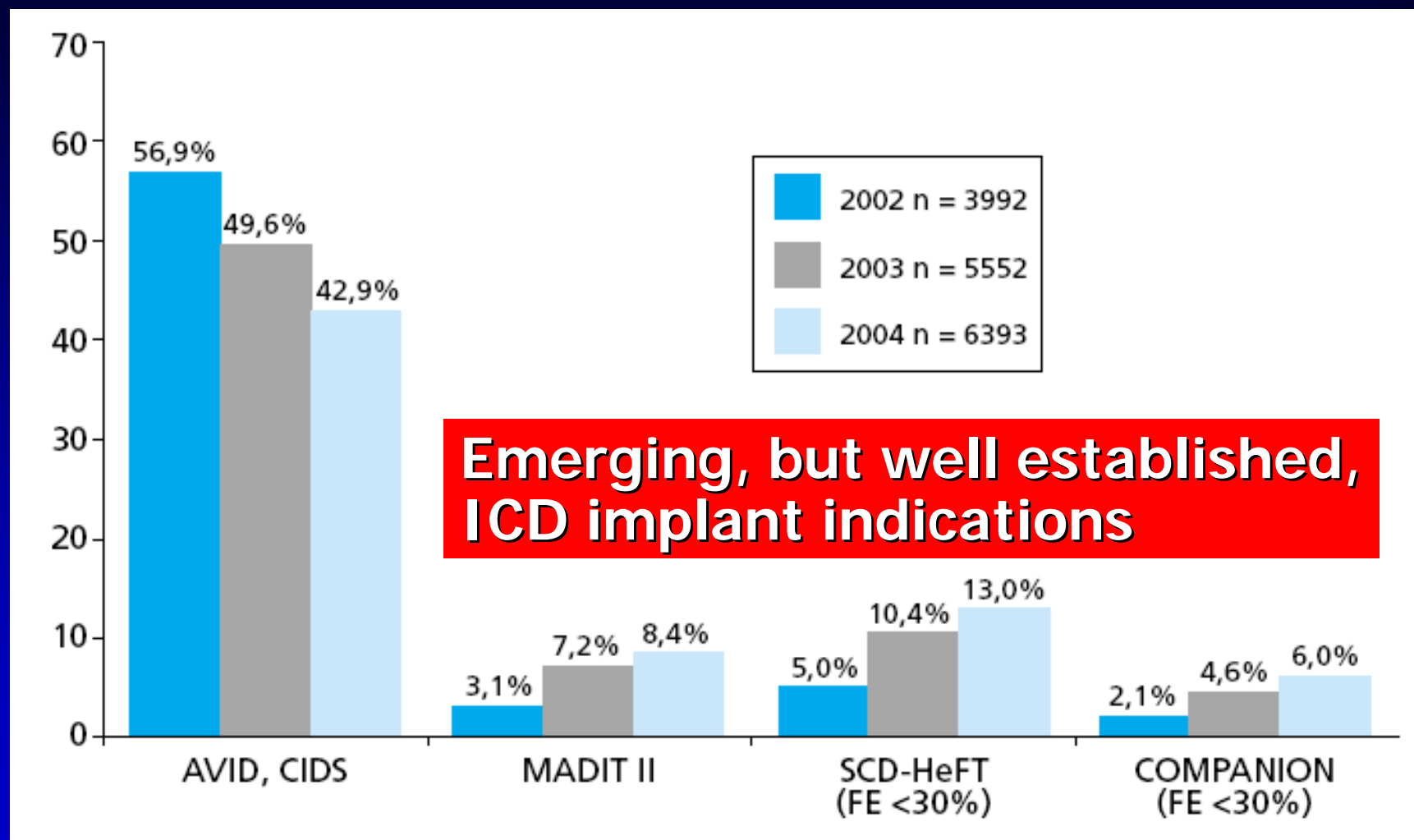
Controversial ICD indications

Italian ICD Implant Rate - EURID form



Proclemer A, AIAC ICD Registry

Controversial ICD indications



Proclemer A, AIAC ICD Registry

The Dark Side of the Moon



Controversial ICD indications:

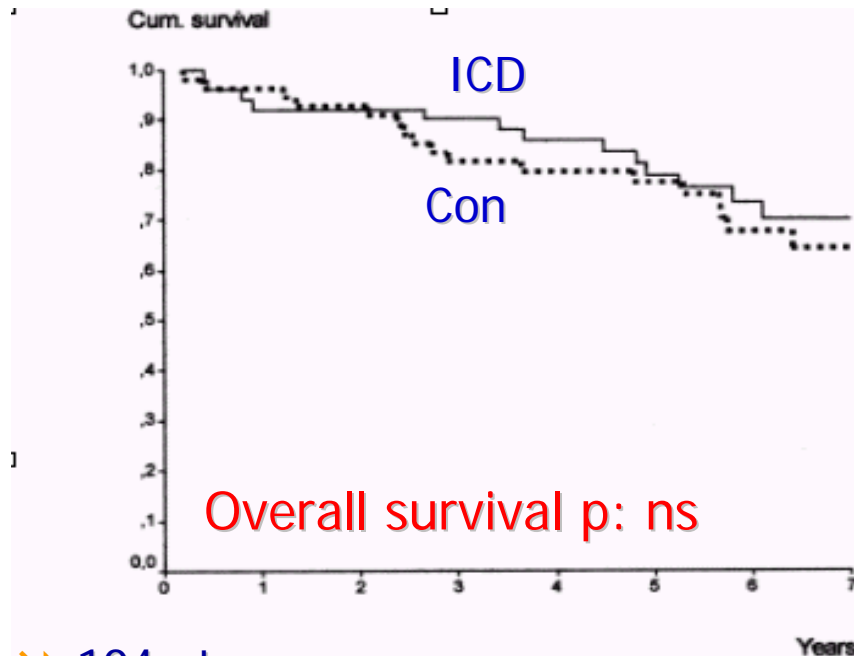
- Conflicting results in randomized trials
- Lack of large randomized trials due to the low prevalence of the disease

Controversial prophylactic ICD indications

- Non-ischemic DCM
- CRT patients
- Inherited Ion Channelopathies (i.e. LQT, SQT, and Brugada syndromes)
- Arrhythmogenic Cardiomyopathies (HOCM, ARVC)

CAT

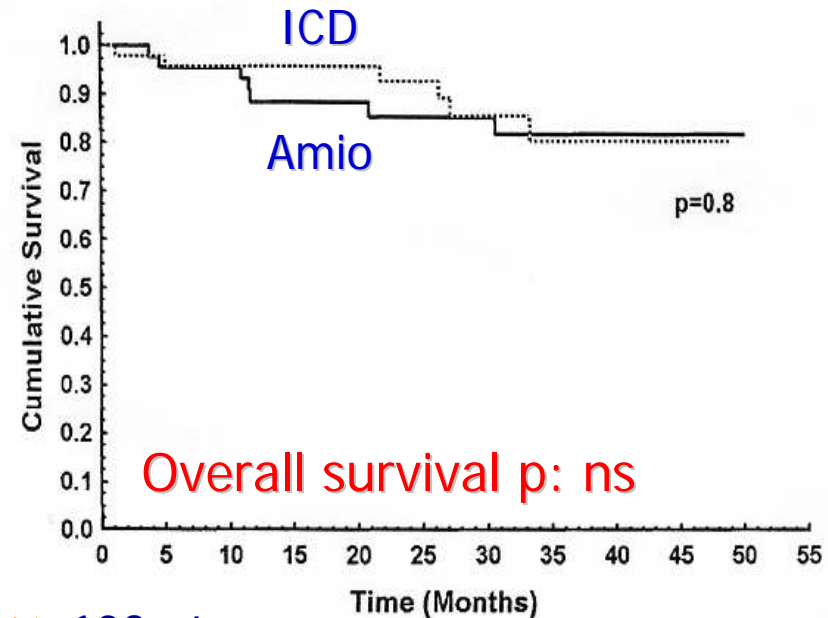
Bansch D, et al.
Circulation 2002;105:1453-58



- 104 pts
- Recent onset (<9 mos) NI-DCM
- EF: $\leq 30\%$
- Trial stopped because the mortality rate (1 yr) did not reach the expected 30%
- Study drawbacks:
 - limited # of pts and FU duration
 - low NYHA Class
 - underusage of β -blockers

AmioVIRT

Strickberger SA, et al.
JACC 2003.43;10:1707-12



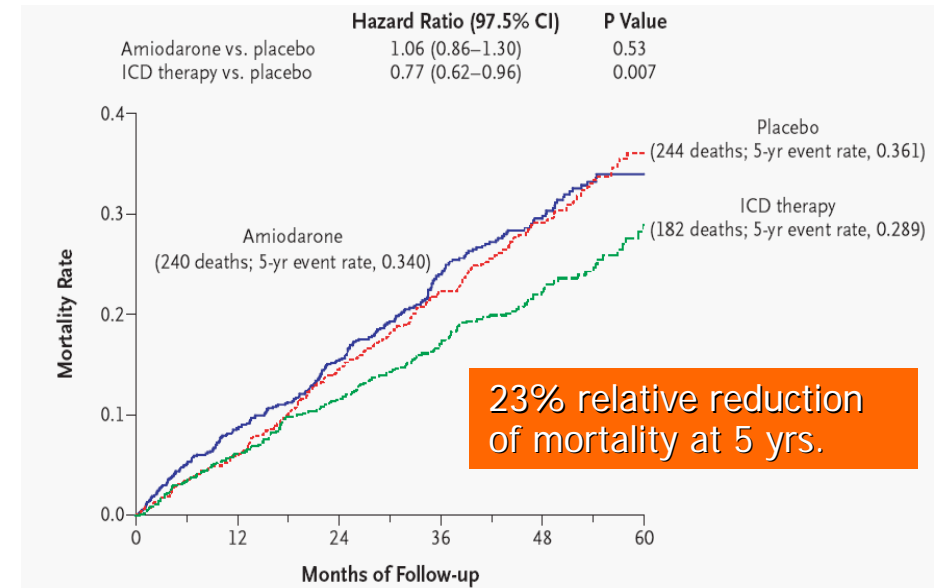
- 103 pts
- NI-DCM
- EF: $\leq 35\%$
- Asymptomatic nSVT
- Study drawbacks:
 - limited # of pts
 - low NYHA Class
 - underusage of β -blockers

SCD-HeFT

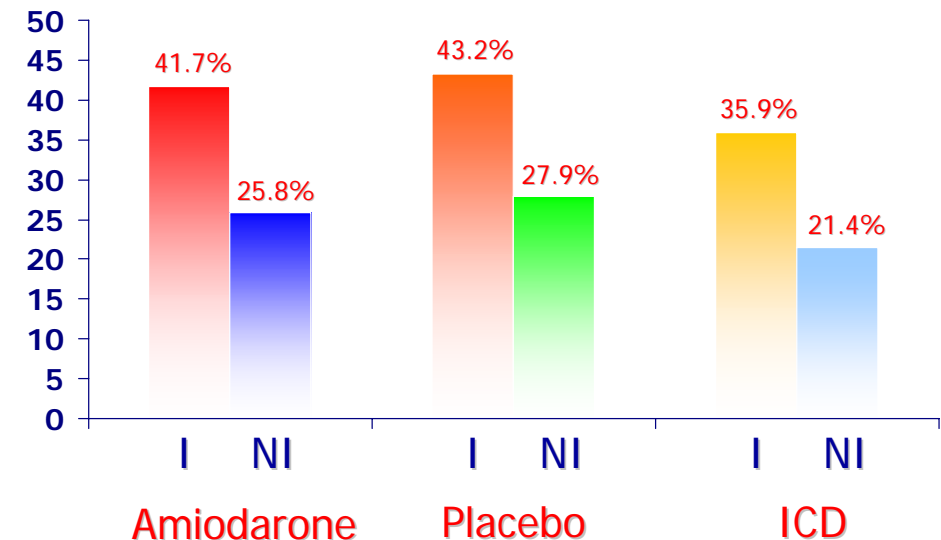
Sudden Cardiac Death in Heart Failure Trial

- 2521 pts
- LV EF: <35%
- NYHA Class: II (70%)- III (30%) despite optimized medical Rx
- Randomization (1:1:1): Med Rx, Amio, ICD
- Primary end-point: total mortality
- Secondary end-points:
 - etiology-related mortality (I-DCM vs NI-DCM)
 - NYHA Class-related mortality
- Follow-up: 45.5 months (median)

Bardy et al, N Engl J Med 2005; 352: 225



Etiology-related mortality



Controversial ICD indications: NI-DCM

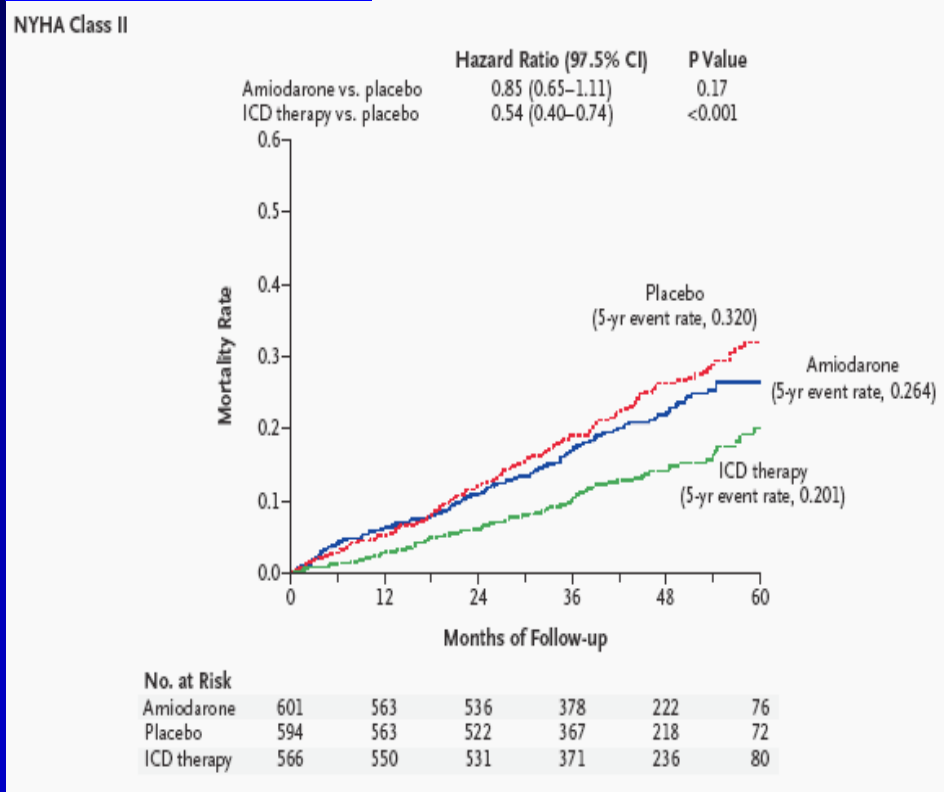
DEFINITE (458 pts, NI-DCM, EF \leq 35%, nSVT)

	Hazard Ratio (95% CI) ICD vs. OMT	P- Value	Reduction in Death w/ICD
Death from Any Cause (All Pts)	0.65 (0.40 - 1.06)	0.08	35%
Death from Any Cause (NYHA Class III)	0.37 (0.15 - 0.90)	0.02	63%
Sudden Death from Arrhythmia	0.20 (0.06 - 0.71)	0.006	80%

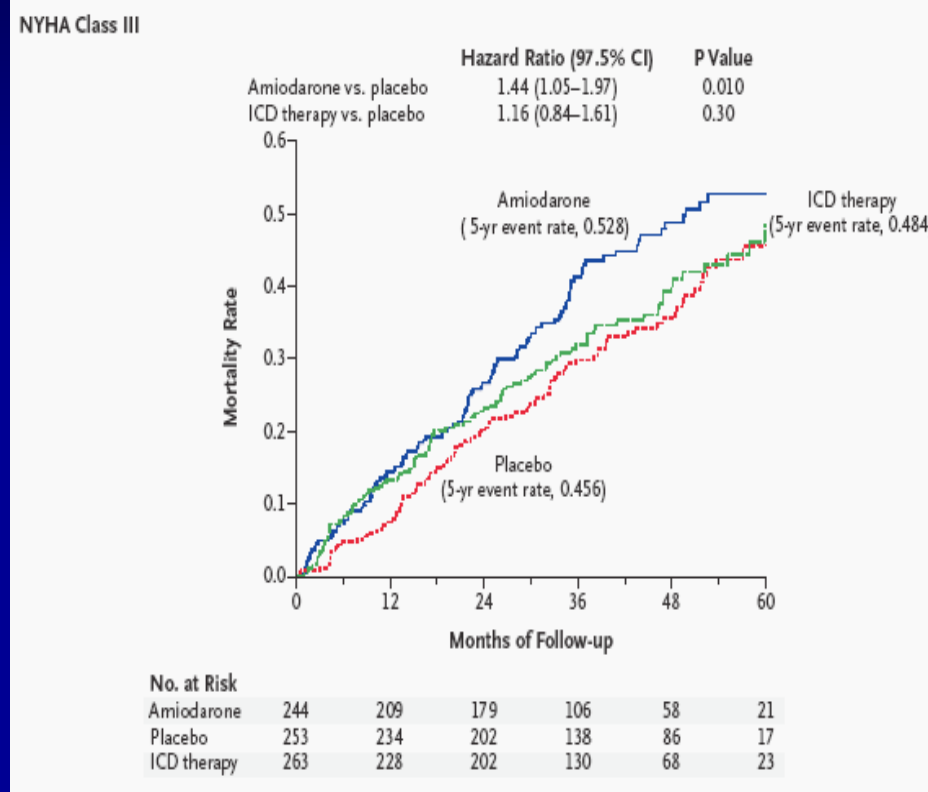
Kadish A. N Engl J Med. 2004;350:2151-2158.

SCD-HeFT: NYHA Class-related mortality

NYHA Class II



NYHA Class III



Bardy et al, *N Engl J Med* 2005; 352: 225

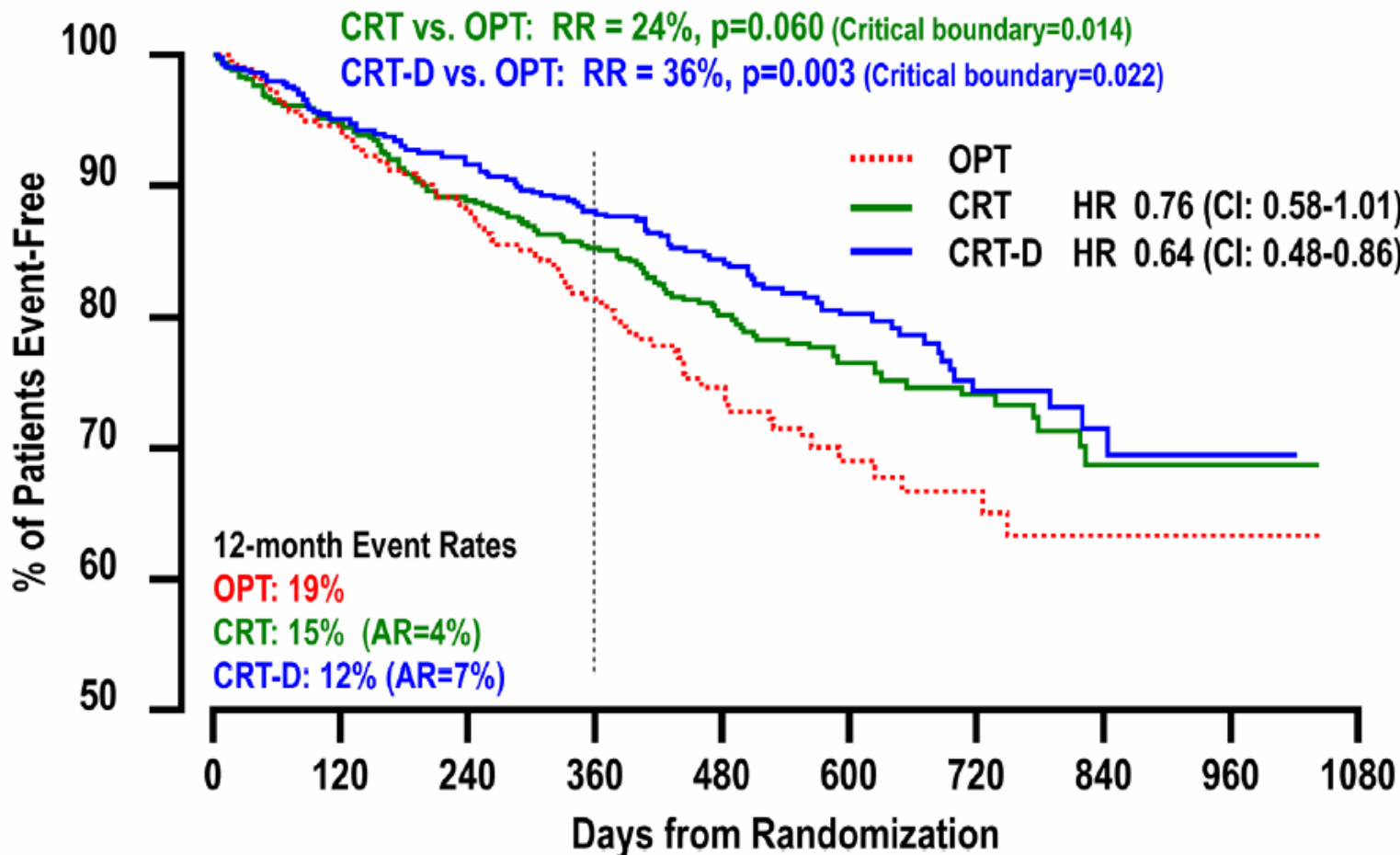
- ↘ Some conflicting evidences of ICD benefit in NI-DCM
- ↘ Implant indication in pts with:
 - LV EF <30%
 - other risk markers (NYHA class, syncope, TWA, etc)

Controversial prophylactic ICD indications (Class II B)

- ↘ Non-ischemic DCM
- ↘ CRT patients
- ↘ Inherited Ion Channelopathies (i.e. LQT, SQT, and Brugada syndromes)
- ↘ Arrhythmogenic Cardiomyopathies (HOCM, ARVC)

COMPANION

Secondary Endpoint of All-Cause Mortality

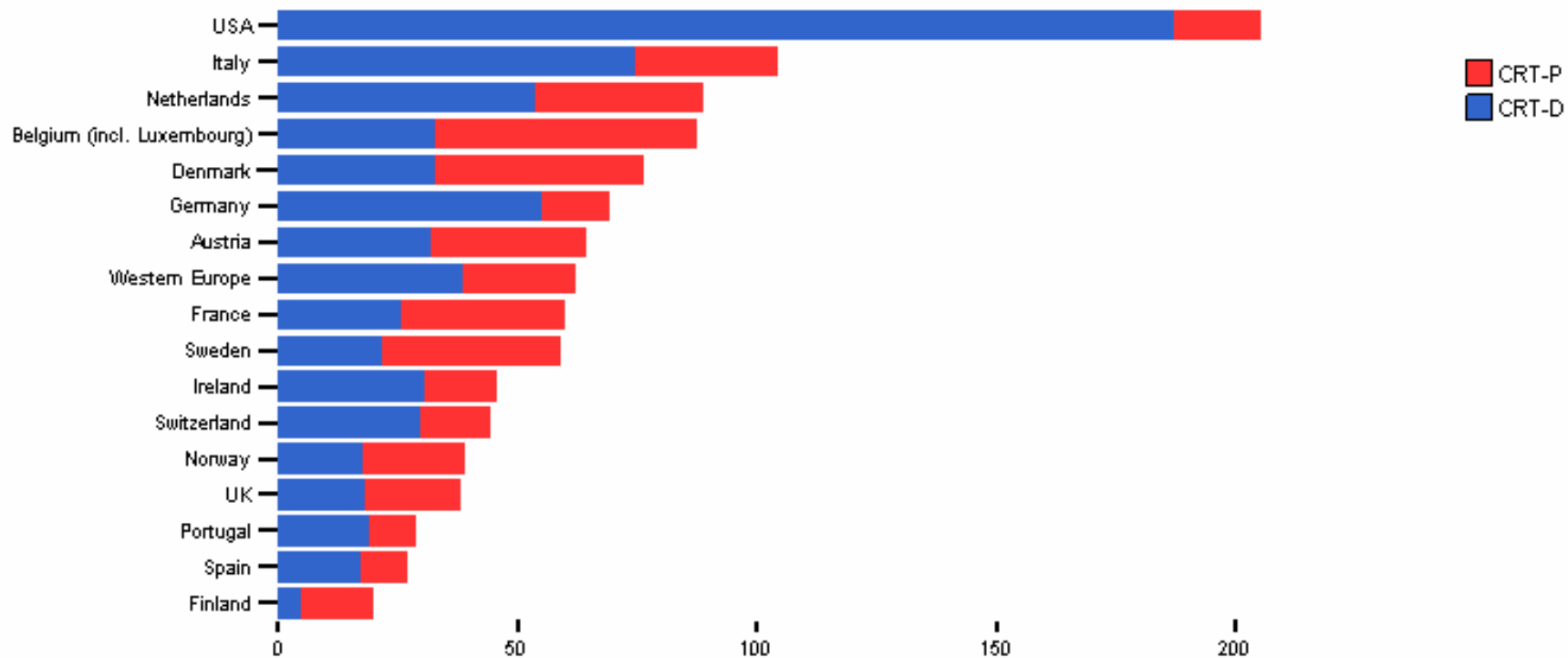


- **Event rate reductions:**

- CRT by 24% (trend, p= .12 vs OPT)
- CRT-D by **36%** (p= .002 vs OPT)

Controversial ICD indications: CRT-P vs CRT-D

CRT-P and CRT-D Implant Rates, 2005



Controversial ICD indications: CRT-P vs CRT-D

Survival improvement

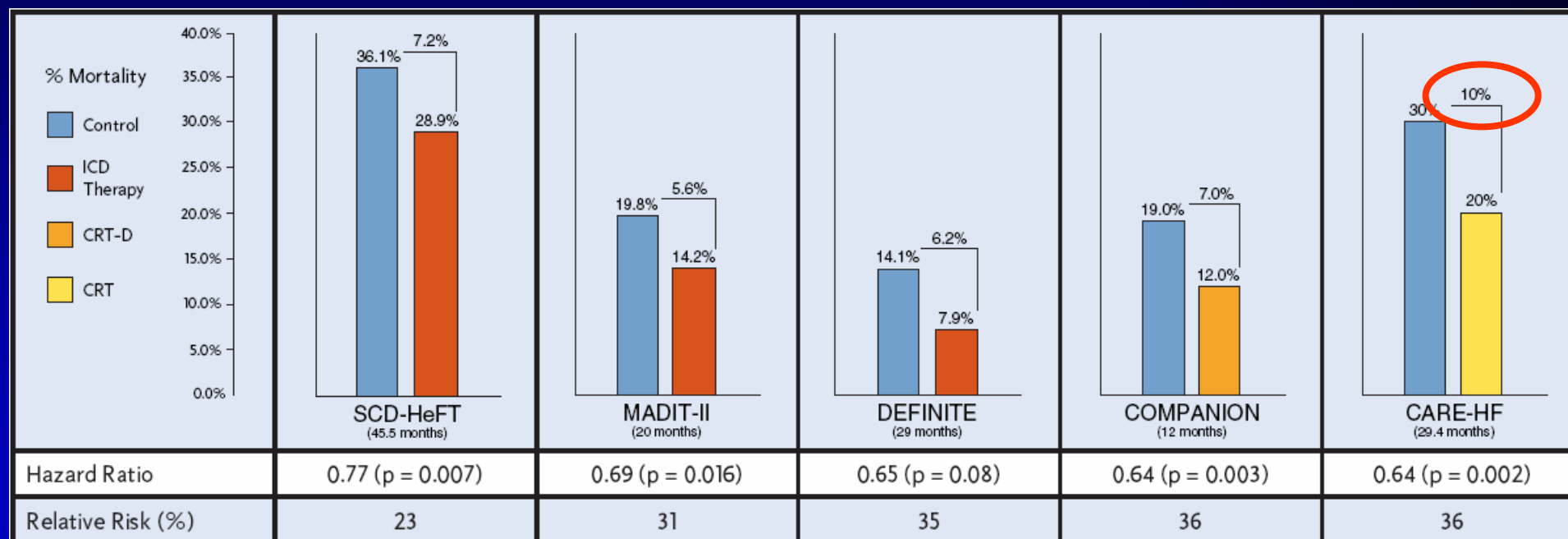
SCD-HeFT

MADIT II

DEFINITE

COMPANION

CARE-HF



23% ↓

31% ↓

35%* ↓

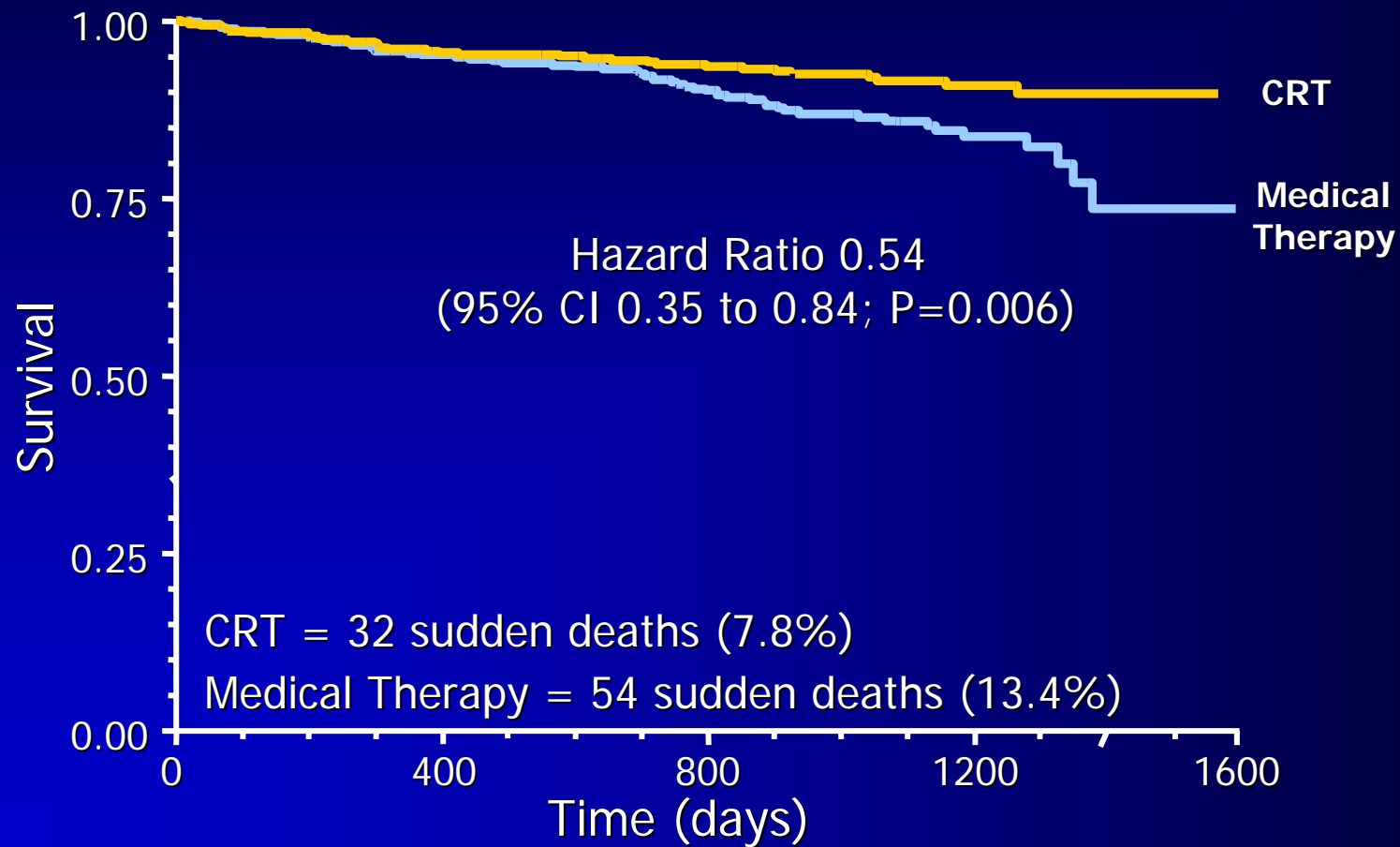
36% ↓

36%† ↓

* p=0.08

† 40% ↓ in the extension phase

CARE-HF Extension Phase



Cleland J, ESC 2005

Controversial ICD indications: CRT-P vs CRT-D

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FOCUS ISSUE: CARDIAC RESYNCHRONIZATION THERAPY

There Is Plenty of Room for Cardiac Resynchronization Therapy Devices Without Back-Up Defibrillators in the Electrical Treatment of Heart Failure

J. Claude Daubert, MD, FACC, Christophe Leclercq, MD, PhD, Philippe Mabo, MD
Rennes, France

Patients with chronic heart failure might benefit from electrical therapy with a view to resynchronize the heart and improve its mechanical performance by cardiac resynchronization therapy (CRT) or to prevent the risk of sudden death by automatic defibrillation. These two therapies can be applied separately or with a combined device, the biventricular implantable cardioverter-defibrillator (CRT-D). There is currently no strong scientific evidence indicating that a CRT-D must be offered to all candidates for CRT. Plain common sense should limit the prescription of these costly devices for patients in need of secondary prevention or for younger patients without major comorbidities. The preferential choice of CRT pacemakers in the remainder of patients is currently a logical one. (J Am Coll Cardiol 2005;46:2204-7)
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Controversial ICD indications: CRT-P vs CRT-D

- ↘ To prove that CRT-D is superior to CRT-P, a new study should be planned
- ↘ To have a statistical power of 90% to detect a 5% absolute relative risk reduction of death from any cause it should enroll:
 - 1.300 patients per group
 - follow-up period equivalent to that of CARE-HF

Daubert, JACC 2005;46:2204 –7

CRT-P might be better:

- Older pts
- Presence of severe co-morbidities
- Patient choice
- Economical restrictions

Quality of death!

Controversial prophylactic ICD indications (Class II B)

- ↘ Non-ischemic DCM
- ↘ CRT patients
- ↘ Inherited Ion Channelopathies (i.e. LQT, SQT, and Brugada syndromes)
- ↘ Arrhythmogenic Cardiomyopathies (HOCM, ARVC)

Controversial ICD indications: LQTS

- β -blocker therapy may significantly improve symptoms occurrence in LQTS pts, but previously symptomatic pts remain at high risk of sudden cardiac death ⁽¹⁾
- The LQTS genotype influences the clinical outcome ⁽²⁾:
 - more frequent cardiovascular events in LQT1 and LQT2 pts
 - higher risk of sudden cardiac death in LQT3 pts (SCN5A mutation)

1. Moss AJ, et al. *Circulation* 2000;101:616-23

2. Zareba W, et al. *N Engl J Med* 1998;339:960-5

Controversial ICD indications: LQTS

Implantable Cardioverter Defibrillator in High-Risk Long QT Syndrome Patients

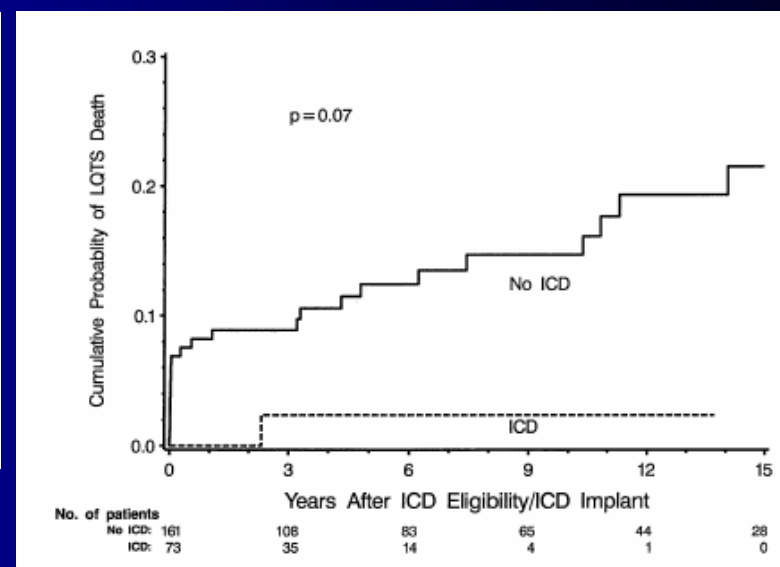
WOJCIECH ZAREBA, M.D., PH.D., ARTHUR J. MOSS, M.D., JAMES P. DAUBERT, M.D., W. JACKSON HALL, PH.D., JENNIFER L. ROBINSON, M.S., and MARK ANDREWS, B.B.A.

From the Cardiology Unit, Department of Medicine, and Department of Biostatistics, University of Rochester School of Medicine and Dentistry, Rochester, New York, USA

ICD in High-Risk LQTS Patients. *Introduction:* Implantable cardioverter defibrillators (ICDs) are increasingly being used in high-risk long QT syndrome (LQTS) patients, but there are limited data regarding clinical experience with this therapeutic modality. The aim of this study is to describe the clinical characteristics of 125 LQTS patients treated with ICDs compared with LQTS patients having similar risk indications who were not treated with ICDs.

Methods and Results: Among 125 LQTS patients with ICDs, there were 54 cardiac arrest survivors, 19 patients who had ICDs implanted due to recurrent syncope despite beta-blocker therapy, and 52 patients with ICDs implanted due to other reasons, including syncope and LQTS-related sudden death in a close family member. Patients with cardiac arrest and those with recurrent syncope despite beta-blocker therapy ($n = 73$) were compared to 161 LQTS patients who had similar indications (89 cardiac arrest and 72 recurrent syncope despite beta-blocker therapy) but did not receive ICDs. Total mortality was the endpoint of the analysis. There was 1 (1.3%) death in 73 ICD patients followed an average of 3 years, whereas there were 26 deaths (16%) in non-ICD patients during mean 8-year follow-up ($P = 0.07$ from log rank test from Kaplan-Meier curves).

Conclusion: ICDs provide an important therapeutic option to prevent sudden arrhythmic death in high-risk LQTS patients. A long-term prospective study is needed to determine the benefit of this therapeutic modality in LQTS patients. (*J Cardiovasc Electrophysiol*, Vol. 14, pp. 337-341, April 2003)



ICD implant might be indicated in:

- Symptomatic pts (syncope, aborted SCD)
- Pts intolerant of β -blockers
- SCN5A mutation (LQT3)
- Family history of SCD

Risk factors in Brugada syndrome

- Symptoms (syncope, aborted SCD)
- Typical ECG pattern (coved type)
- Ventricular vulnerability?

No data available to support ICD indication except for symptomatic pts

Controversial prophylactic ICD indications (Class II B)

- ↘ Non-ischemic DCM
- ↘ CRT patients
- ↘ Inherited Ion Channelopathies (i.e. LQT, SQT, and Brugada syndromes)
- ↘ Arrhythmogenic Cardiomyopathies (HOCM, ARVC)

Controversial ICD indications: HOCM

Risk Factor	RR	(95% CI)
Exercise BP	2.4	(1.0–5.5)
Syncope	2.0	(0.8–4.9)
Non-sustained VT	1.8	(0.7–4.7)
Family history of sudden death	1.9	(0.8–4.1)
LV wall thickness >30 mm	4.1	(1.7–9.5)

Risk Score (No. of Risk Factors)	6-Year Sudden Cardiac Death Risk
0	5% (1%–9%)
1	7% (1%–13%)
2	18% (4%–33%)
3	35% (25%–100%)

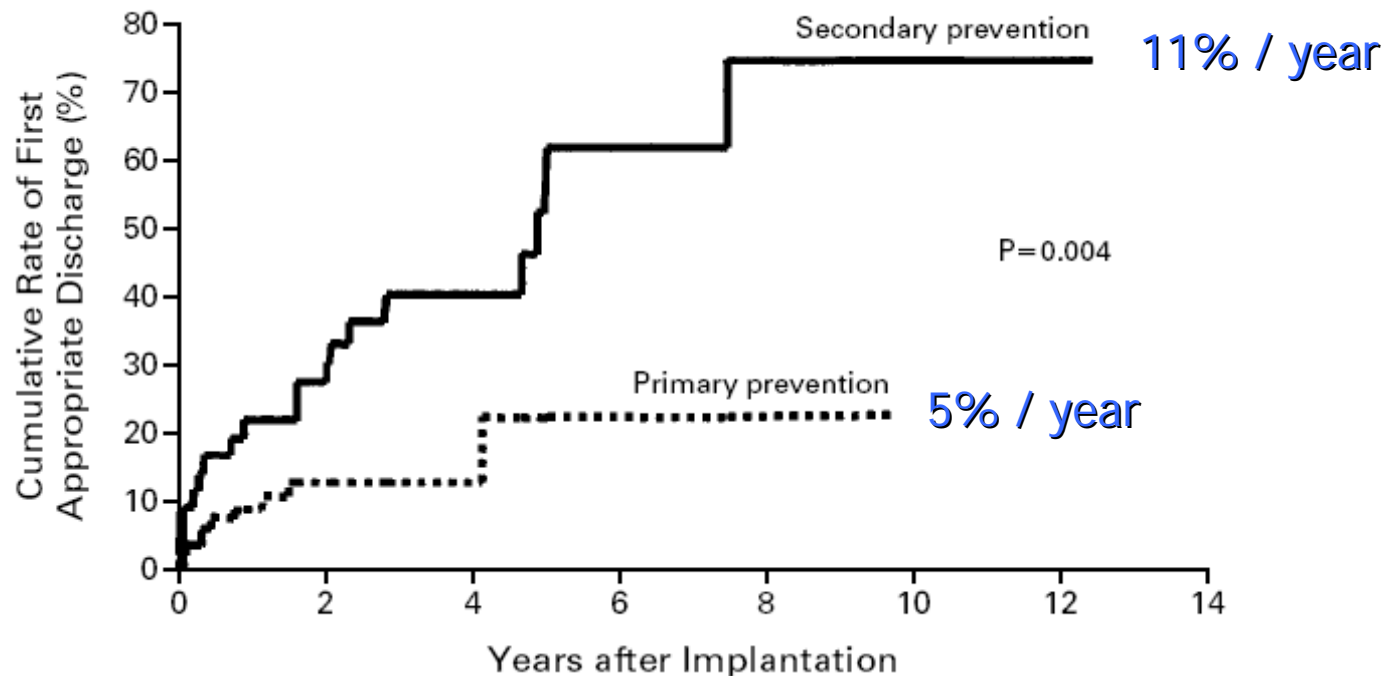
About 50% of SCD pts have no risk factors

Elliot PM, et al. JACC 2000;36:2212-8

Controversial ICD indications: HOCM

EFFICACY OF IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS FOR THE PREVENTION OF SUDDEN DEATH IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY

BARRY J. MARON, M.D., WIN-KUANG SHEN, M.D., MARK S. LINK, M.D., ANDREW E. EPSTEIN, M.D., ADRIAN K. ALMQUIST, M.D., JAMES P. DAUBERT, M.D., GUST H. BARDY, M.D., STEFANO FAVALE, M.D., ROBERT F. REA, M.D., GIUSEPPE BORIANI, M.D., N.A. MARK ESTES III, M.D., AND PAOLO SPIRITO, M.D.*



N Engl J Med 2000; 342:365-73

Risk factors in ARVC

Previous cardiac arrest

Syncope or sustained ventricular tachycardia with impairment of consciousness

Increased QT dispersion (a difference of ≥ 40 ms between the maximum and minimum QRS values occurring in any of the 12 electrocardiographic leads)

Early onset of symptoms

Severe right ventricular dilatation

Right heart failure

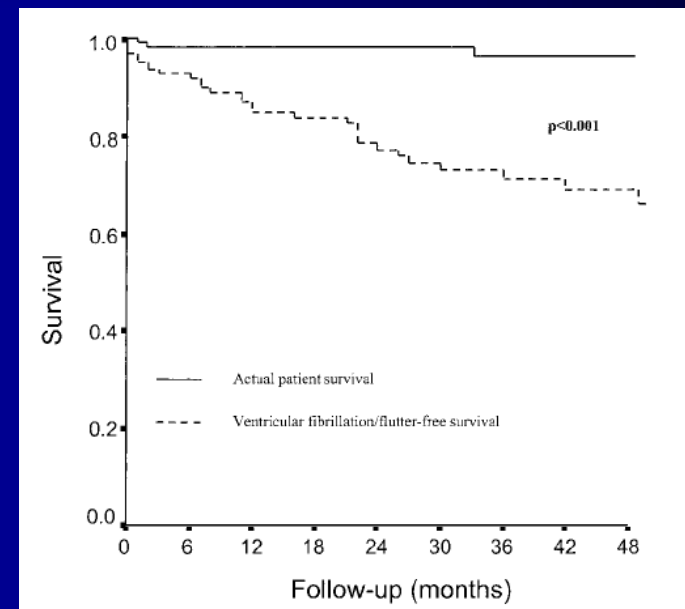
Left ventricular involvement (regional wall motion abnormalities or dilatation and impairment of left ventricular systolic function)

Controversial ICD indications: ARVC

Implantable Cardioverter-Defibrillator Therapy for Prevention of Sudden Death in Patients With Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia

Domenico Corrado, MD, PhD; Loira Leoni, MD; Mark S. Link, MD; Paolo Della Bella, MD; Fiorenzo Gaita, MD; Antonio Curnis, MD; Jorge Uriarte Salerno, MD; Diran Igidbashian, MD; Antonio Raviele, MD; Marcello Disertori, MD; Gabriele Zanolto, MD; Roberto Verlato, MD; Giuseppe Vergara, MD; Pietro Delise, MD; Pietro Turrini, MD, PhD; Cristina Basso, MD, PhD; Franco Naccarella, MD; Francesco Maddalena, MD; N.A. Mark Estes III, MD; Gianfranco Buja, MD; Gaetano Thiene, MD

- ICD effective in symptomatic pts
- No data available in asymptomatic pts



Circulation 2003;108:3084-91

Conclusions

Data gathered from large, randomized, multicenter studies has resulted in an exponential rise of the ICD implant rate.

Nonetheless, some debates or controversies still exist regarding the role of prophylactic ICD implant in selected patient subsets.

Some of these issues might be addressed by future studies.

A decision-making based on the clinical good-sense and patient choice should be adopted in controversial situations.